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EFFECT OF SMOKING AND OBESITY ON THE SERUM LEVELS OF VITAMIN D3 IN THE CENTRAL REGION OF JORDAN

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ABSTRACT

The aim of this study is to determine the levels of Vitamin D3 in the province of Russeifa-Jordan and to clarify the effect of demographic variables on Vitamin D3concentration.

A cross-sectional study was conducted in the period of April 2016 up to August 2018 in Al-Russeifa, Jordan. Two hundred and seventy-eight subjects were enrolled in this study; 211 females and 67 males, among them 168 nonsmokers and 110 smokers.

Vitamin D3 levels ranged from 2 to 36 ng/ml with a mean of 17.37 ± 7.23 ng/ml. Ages ranged from 2 years to 80 years with a mean of 36.3 ± 12.7. Vitamin D3 levels were higher in males than females 19.11 ± 7.399 and 16.82 ± 7.110 ng/ml, respectively.75% of the study population suffered from insufficiency, 20% were obeying sever deficiency levels and only 5% showed sufficient levels of Vit. D3. Negative correlation was demonstrated between smoking, BMI and

Vit D3serum levels (r= -0.324, p<0.01)(r= - 0.229 p<0.001), respectively. Smoking, age, and BMI are inversely associated with low levels of vitamin D3 in the Jordanian population.

Keywords: Vitamin D3, Obesity, Smoking, Age, Gender, Russeifa, Jordan

INTRODUCTION

The recent growing mass of data has revealed the association of Vitamin D deficiency and insufficiency with multiple diseases and disorders (Dzik & Kaczor, 2019). Preliminary studies have established vitamin D critical effect on optimal bone mineral density influenced by renal and intestinal resorption of calcium and phosphate (Carmeliet, Dermauw, & Bouillon, 2015). Nevertheless, the widespread distribution of vitamin D receptor (VDR), which is one of the nuclear steroid hormone receptors, supported the evidence for the pleiotropic effects of vitamin D which is more than a bone hormone (Wang, Zhu, & DeLuca, 2012).

The main two isoforms of vitamin D, are the biologically active vitamin D3 (cholecalciferol), described as "the sunshine vitamin", and vitamin D2 (ergocalciferol) that can be endogenously synthesized in the skin using the energy of ultraviolet B (UVB). In addition, vitamin D3 can be obtained exogenously from dietary sources or supplements(Macdonald et al., 2011). Vitamin D supply is quite variable that varies according to: life style, genetic, environmental factors (Bouillon, 2017; X. Jiang et al., 2018; Macdonald et al., 2011). Vitamin D sufficiency is critical during children growth and adolescents not only for optimal bone health but also extra-skeletal functions. Many researchers have described the negative impact of inadequate serum levels of Vitamin D on bone rickets in children and osteoporosis in adults (Ahmadieh & Arabi, 2011). Vitamin D insufficiency is associated with many pathological disorders such as cases of hypertension (Gislefoss et al., 2018; Jia et al., 2014), chronic kidney disease (CKD) (Yoshihara, Kaneko, Iwasaki, Nohno, & Miyazaki, 2018), common cancers (van Duijnhoven et al., 2018), cardiovascular disease (Mallah et al., 2018), improper immune modulation and asthma (Chinellato et al., 2018). Additionally, Vitamin D has been implicated with the maintenance of human health and neurological development in both fetal and adults brain (Brum, Comini-Frota, Vasconcelos, & Dias-Tosta, 2014). On the other, scientists have linked high vitamin D levels with a healthier lipid profile and a

better life quality (Jungert, Roth, & Neuhauser-Berthold, 2015).

Tobacco smoking and obesity has been considered as a burden on health impact. Reducing those two independent and or combined factors may be motivated as it has been associated with reducing risk factors of morbidity and mortality (Freedman et al., 2015; Lavie, Carbone, Kachur, O'keefe, & Elagizi, 2019; Underner, Peiffer, Perriot, Harika-Germaneau, & Jaafari, 2018).

Tobacco smoking is a deleterious habit which harbors more than 5000 chemicals delivered directly to the lung, many of which are known to be toxic and carcinogenic (Abu Rayyan, 2016a; Heulens et al., 2015). Smoking hinders the homeostasis of different biological systems like the cardiovascular system, respiratory system, wound healing activity, and body regeneration mechanism (Abu Rayyan, 2016b; Talhout et al., 2011).

It has been revealed lately that Vitamin D levels can mainly been indomitable by Tobacco smoking and high BMI (Kassi et al., 2015; Li et al., 2018). Several publications have listed Jordan in countries with hypovitaminosis D in the blood stream among Jordanian citizens (Al Haj Ahmad & Al-Domi, 2017; Alkhatatbeh, Abdul-Razzak, Khasawneh, & Saadeh, 2017; Jarrah et al., 2018). From geographical demography, Jordan is lined on the Saturn altitude with adequate sunlight exposure during the year and the majority of the Jordanian citizens are above the line of poverty. Consequently, we addressed a question about the factors which conferred this depletion in Vit. D levels.

Literature reviews, found most of the Vitamin D studies were conducted on elderly and hospitalized patients while the information on youth and middle-aged people are limited (Kassi et al., 2015). Additionally, paucity of information about the correlation of vitamin D levels with other demographic parameters as smoking, gender and BMI in the middle region of Jordan, in specific has enthused us to conduct this study. We will try to elucidate the impact of smoking and other demographical factors as gender and body mass index on Vitamin D levels in that area.

2. MATERIALS AND METHODS

2.1. Study Population

This cross-sectional study was conducted in the period of April 2016 up to August 2018 in Al-Russeifa, Jordan. Two hundred and seventy-eight subjects were enrolled in this study; 211 females and 67 males, among them 168 nonsmokers and 110 smokers. Research committee at the Faculty of Pharmacy and Medical Sciences, Al-Ahliyya University, Amman, Jordan has authorized

the protocol of the study and the Baseline information form (December 2017). The Baseline information form included questions about age, gender, body mass index (BMI), smoking, and vitamin D3 supplements intake. Subjects under supplements medication of vitamin D3 were eliminated from the study.

2.2. Blood Phlebotomy

Blood samples were drawn from the brachial vein using 5 mL syringes, transferred into 10 mL plane test tube, allowed to clot at room temperature, and then centrifuged at 5000 rpm for 3 minutes. Serum was transferred to a plane tube and stored at −70◦ C until for further analysis. Each subject has filled the case report form before the blood sampling.

2.3. Measurement of Vitamin D3:

Quantitative colorimetric immunoenzymatic determination of 25(OH) vitamin D3 concentrations in human plasma level were developed by using vitamin D3 ELISA kit (Diametra, Milano, Italy). The kit is a competitive solid phase enzyme-linked immunosorbent assay (ELISA). Samples were analyzed according to the manufacturer guidelines.

2.4. Vitamin D3 Classifications.

We have adopted the Classification of American Geriatric Society (AGS) for Vitamin D3 levels(Dawson-Hughes, 2014)which classify Vit D into 3 major groups according to as follows: (1) sufficient (>30 ng/mL); (2) insufficient (10–30 ng/mL); (3) deficiency (<10 ng/ml) (American Geriatrics Society Workgroup on Vitamin D Supplementation for Older Adults, 2014).

Statistical analysis

Data were expressed as M ± SD. The SPSS program version 25 was used in the analysis. One-way analysis of variance (ANOVA) followed by Duncan post hoc test and/or t-test was used in the analysis. Pearson correlation coefficient was used to study correlations. P-values less than 0.05 was significant.

A Spearman's rho correlation was used to analyze the association between non-normally distributed variables.

Correlations between normally distributed variables were analyzed by Pearson's correlation coefficient. A p-value of < 0.05 was considered statistically significant.

RESULTS

278 volunteers have enrolled in the study, 67male and 211female ages ranged from 2 years to 80 years with a mean of 36.3 ± 12.7, among them 168 nonsmokers and 110 smokers, Vitamin D3 levels ranged from 2 to 36 ng/ml with a mean of 17.37±7.23 ng/ml summarized in Table 1. Vitamin D3 levels were higher in males than females 19.11 ±

7.399 and 16.82 ± 7.110 ng/ml, respectively (Table 1, Figure 1a).

Smoking

Vitamin D3 levels were higher in nonsmokers compared with smokers with a mean of 19.26 ±6.97 and 14.48±6.665 ng/ml, respectively (Table1, Figure 1a). Vitamin D3levels were higher in male's nonsmokers compared with female's nonsmokers whereas there was no difference in Vitamin D3 levels in both genders in smoker's category (figure 1b)A negative correlation was found between both smoking and vitamin D3 levels (r= -0.324, p< 0.001) (Table 2).

BMI

The underweight group showed higher Vit. D3 levels than obese groups 24.58 ± 6.86 ng/ml and 13.98± 2.57 ng/ml, respectively (Table1, Figure 2a). Around 35 % of the study population were located in the obese and sever obese category with a mean of 15.15± 2.57 ng/ml. There was a significant decrease in Vitamin D3 levels with an increase of BMI (Figure 2b). A negative correlation was found between both BMI and vitamin D3 levels (r=-0.229, p< 0.001) (Table 2).Additionally, Vitamin D3levels were lower in females with high BMI status (Figure 2b)

Age

Vitamin D3 levels were higher in the younger agesin comparison with older ages22.55 ± 7.67 ng/ml, 15.47± 3.16 ng/ml, respectively (Table 1, Figure 3a).A significant decrease in the levels of Vit. D3 was demonstrated with the increase of age p< 0.05 (Table1). A significant correlation was demonstrated between age and BMI levels (Table 2). Vitamin D3 levels were significantly lower in older ages females (Figure 3b)

Multiple linear regression analysis revealed that BMI and smoking accounted for 10% and 27% of the serum Vit. D3 level variability in the total population inthe two subgroups (< 18.5 underweight and 18.5 - 25 normal)(Table 3), respectively, while only smoking was a significant determinant of serum Vit. D3 for 25 - 30 overweight. Interestingly, Vit. D3 level was lower by approximately 4.8 ng/dl in a smoker compared to a non-smoker for the total population and the (< 18.5 underweight, 18.5 - 25 normal and 25 - 30 overweight subgroup (p<0.001, and p=0.012, p=0.03, and p<0.050, p= respectively).

The multinomial logistic regression model for the association between demographic characteristics and Vit. D3 levels demonstrated that BMI and smoking had a 4.5 % and 13% for the increased likelihood

of having vitamin D3 deficiency compared to a non-smoker and <18 weight for the deficiency and insufficiency subgroup (p=0.002 and p< 0.001) (Table 4).

Table 1: Demographic characteristics of the study population

		N	Mean	*P*	
Smoking	Nonsmoker	168	19.26 ±6.97	0.001	
	Smoker	110	14.48±6.66		
Sex	Female	211	16.82±7.11		
	Male	67	19.11±7.39	0.024	
			Subset for alpha = 0.05		
			1	2	3
BMI	> 35 sever obesity	31	13.98[a]		
	30 - 35 obese	66	16.31[a]	16.31[a,b]	
	18.5 - 25 normal	68		17.32[b]	
	25 - 30 overweight	90		18.02[b]	
	< 18.5 under weight	23			22.55[c]
Age	70-80	15	15.47[a]		
	40-49 years	51	15.86[a]		
	20-29 years	55	16.37[a]		
	30-39 years	63	16.87[a]		
	60-69 years	17	18.04[a]		
	50-59 years	29	19.62[a]	19.62[a,b]	
	11-19 years	48		24.16[b]	24.16[b,c]

A,b,c Post hoc Duncans analysis

Table 2: The correlation between vitamin D3levels and demographical characteristics

		BMI	Sex	Age	Smoking	Vit.D3
BMI	Pearson Correlation	1	-0.06	.241**	0.069	-.229**
	Sig. (2-tailed)		0.358	0.001	0.254	0.001
	N	278	278	278	278	278
Sex	Pearson Correlation		1	0.006	-0.043	.136*
	Sig. (2-tailed)	-		0.915	0.473	0.024
	N		278	278	278	278
Age	Pearson Correlation			1	0.111	-0.1
	Sig. (2-tailed)	-	-		0.065	0.088
	N			278	278	278
Smoking	Pearson Correlation				1	-.324**
	Sig. (2-tailed)	-	-	-		0.001
	N				278	278
Vit.D3	Pearson Correlation					1
	Sig. (2-tailed)	-	-	-	-	
	N					278

Bold indicates statistical significant correlation * p<0.05 **

Table 3: Multiple linear regression model for the association between demographic and clinical characteristics and levels of Vitamin D3

Vit_D3_1[a]		B	Df	Sig.	Exp(B)	95% Confidence Interval for Exp(B)	
						Lower Bound	Upper Bound
Sever Deficiency	Intercept	-1.367	1	.415			
	BMI	2.731	1	.000	15.351	4.696	50.179
	Sex	-1.323	1	.108	.266	.053	1.339
	Age	.016	1	.940	1.016	.678	1.522
	[Smoking=1]	-2.109	1	.010	.121	.024	.607
	[Smoking=2]	0[b]	0	.	.	.	.
Insufficiency	Intercept	-1.362	1	.378			
	BMI	2.795	1	.000	16.358	5.140	52.061
	Sex_1	-.653	1	.371	.521	.125	2.176
	Age_1	.028	1	.884	1.028	.709	1.491
	[Smoking=1]	-1.250	1	.109	.286	.062	1.321
	[Smoking=2]	0[b]	0	.	.	.	.

a. The reference category is: Sufficiency.
b. This parameter is set to zero because it is redundant

Table 4: The multinomial logistic regression model for the association between demographic characteristics and Vit. D3 levels

BMI		B	Df	Sig.	Exp(B)	95% Confidence Interval for Exp(B)	
						Lower Bound	Upper Bound
< 18.5 under weight	Intercept	19.406	1	.980			
	Sex	-.070	1	.930	.932	.195	4.463
	Age	-.473	1	.012	.623	.432	.900
	Smoking	-.038	1	.954	.963	.267	3.475
	[Vit_D3_1=1]	-17.524	1	.982	2.43E-8	.000	.[b]
	[Vit_D3_1=2]	-17.819	1	.982	1.86E-8	.000	.[b]
	[Vit_D3_1=3]	0[c]	0	.	.	.	.
18.5 - 25 normal	Intercept	17.815	1	.982			
	Sex_1	.656	1	.230	1.927	.660	5.623
	Age_1	-.387	1	.003	.679	.525	.878
	Smoking	-.431	1	.349	.650	.263	1.603
	[Vit_D3_1=1]	-15.438	1	.984	1.93E-7	.000	.[b]
	[Vit_D3_1=2]	-15.219	1	.985	2.48E-7	.000	.[b]
	[Vit_D3_1=3]	0[c]	0	.	.	.	.
25 - 30 over weight	Intercept	2.480	1	.998			
	Sex	.186	1	.727	1.205	.424	3.421
	Age	-.134	1	.267	.875	.690	1.108
	Smoking	-.854	1	.050	.426	.181	1.000
	[Vit_D3_1=1]	-.025	1	1.00	.975	.000	.[b]
	[Vit_D3_1=2]	.445	1	1.00	1.560	.000	.[b]
	[Vit_D3_1=3]	0[c]	0	.	.	.	.
30 - 35 obese	Intercept	1.683	1	.134			
	Sex_1	.177	1	.748	1.194	.405	3.520
	Age	-.048	1	.699	.953	.746	1.217
	Smoking	-.791	1	.082	.454	.186	1.104
	[Vit_D3_1=1]	-.215	1	.699	.806	.271	2.400
	[Vit_D3_1=2]	.416	1	.	1.516	1.516	1.516
	[Vit_D3_1=3]	0[c]	0	.	.	.	.

a. The reference category is: > 35 severe obesity.
b. Floating-point overflow occurred while computing this statistic. Its value is therefore set to system missing.
c. This parameter is set to zero because it is redundant.

Model Fitting Information

Model	Model Fitting Criteria		Likelihood Ratio Tests	
	-2 Log Likelihood	Chi-Square	df	Sig.
Intercept Only	434.281			
Final	355.849	78.432	20	.000

Likelihood Ratio Tests

Effect	Model Fitting Criteria	Likelihood Ratio Tests		
	-2 Log Likelihood of Reduced Model	Chi-Square	Df	Sig.
Intercept	355.849[a]	.000	0	.
Sex	358.756	2.906	4	.574
Age	373.202	17.353	4	.002
Smoking	361.709	5.860	4	.210
Vit D3	408.149	52.300	8	.000

The chi-square statistic is the difference in -2 log-likelihoods between the final model and a reduced model. The reduced model is formed by omitting an effect from the final model. The null hypothesis is that all parameters of that effect are 0.
a. This reduced model is equivalent to the final model because omitting the effect does not increase the degrees of freedom.

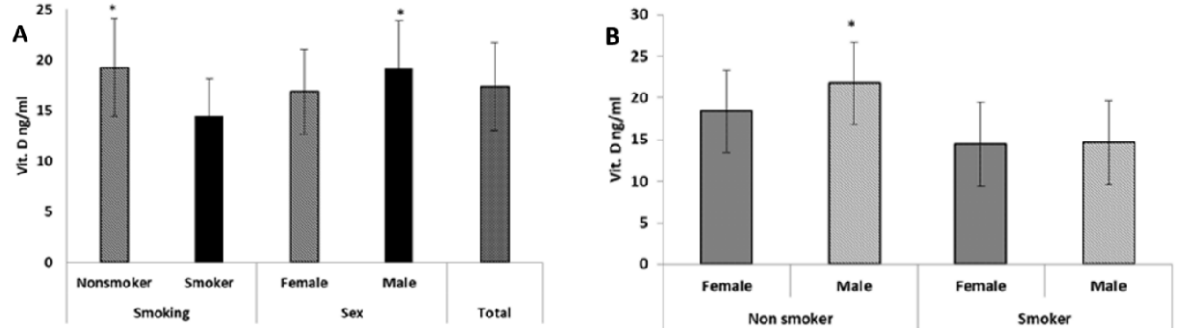

Figure 1: Mean Vitamin D3 concentration in the population study

A: Vitamin D3 levels groups classified according to gender and smoking in different age categories. * Statistically significant (P<0.05). B: Mean Vitamin D3 concentration comparison between the study population according to smokers and nonsmoker's females and males. The difference between nonsmoker males and females is statistically significant (P<0.05) whereas there is no contribution to the gender in Vitamin D3 level for smokers

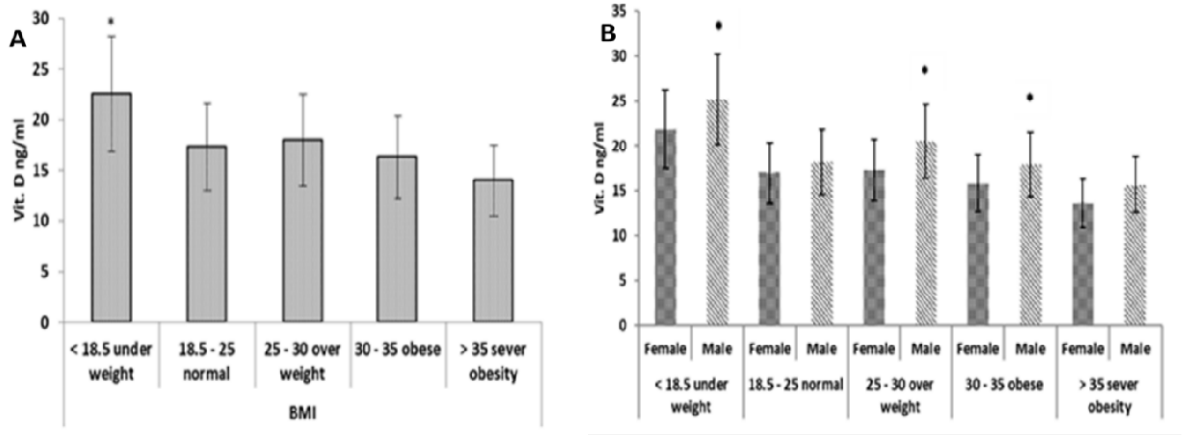

Figure 2: Mean Vitamin D3 concentration in the population study showing Vitamin D3 levels classified according to the body mass index.

A: There is a descending trend in Vitamin D3 levels in relationto the increase of BMI. * statistically significant (P<0.05). B:Distribution of Vitamin D3 in the study population showing Vitamin D3 levels according to the body mass index classified according to gender. * statistically significant (P<0.05).

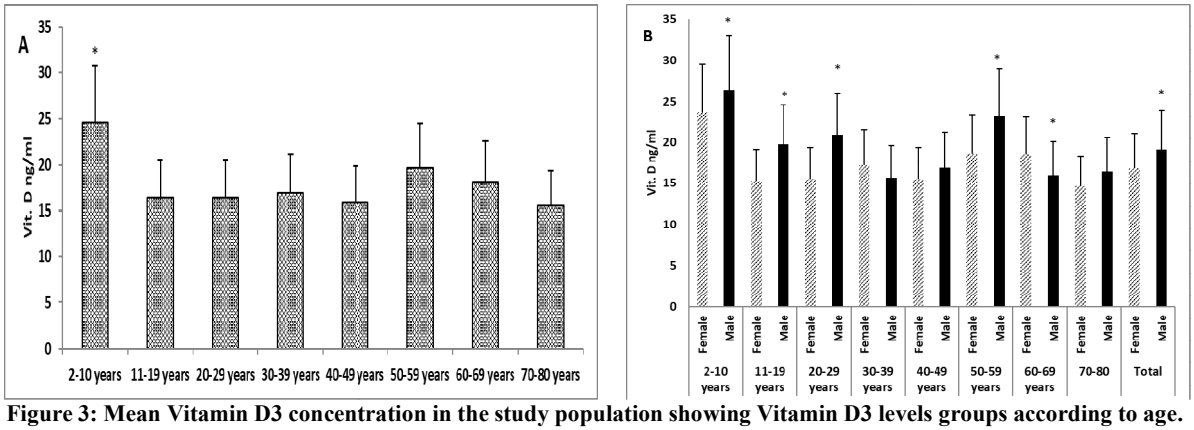

Figure 3: Mean Vitamin D3 concentration in the study population showing Vitamin D3 levels groups according to age. A: There is a decreasing trend in Vitamin D3 levels in comparison with the increase of age * statistically significant (P<0.05). B: Mean Vitamin D3 concentration in the study population showing Vitamin D3 levels for females and males classified according to age. Male levels were higher than females in different age groups. * Statistically significant (P<0.05).

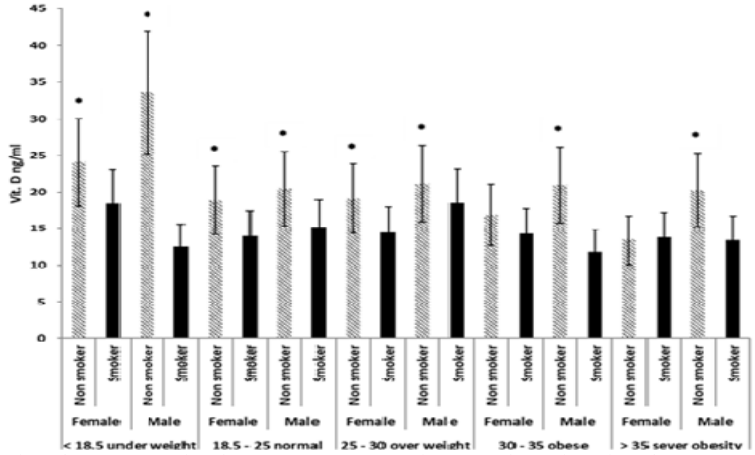

Figure 4: Mean Vitamin D3 concentration in the study population showing Vitamin D3 levels classified according to the body mass index in females or males in relation to the smoking habit. There is a statistically significant decrease correlation between vitamin D3levels in the two categories of nonsmokers and smokers regardless of the gender and the body mass index. (*= p< 0.05)

DISCUSSION

Our study has revealed a low status of Vitamin D3in the study population compared to other published studies as mean Vitamin D3 level was 17.37 ± 7.234 ng/ml. Astonishingly, 75% of the study population suffered from insufficiency, 20% were obeying sever deficiency levels and only 5% showed sufficient levels of Vit. D. Actually, we were shocked and confused about these results, especially neither the geographical location of Jordan nor food intakes were reported as a causative factor for such paucity. By conducting a comparison with studies concerning Vitamin D3 levels in Jordan and other countries; a similar deficiency was noticed, Horanietal reported a mean level of 20 ± 5.4 ng/ml for a population of university students (Al-Horani et al., 2016). Similarly, Atoumetal showed a mean level of 21.8 ng/ml for the control group (Atoum, AlKateeb, & AlHaj Mahmoud, 2015).Likewise, Nicholas et al showed 19.8% deficiency (<12 ng/ml) and 56.5% insufficiency (<20 ng/ml) for 1077 Jordanian children of preschool age (Nichols et al., 2015). In Saudi Arabia, a low level of 3.6 ng/mL (9 nmol/mL) was reported in elderly citizens(Ardawi, Sibiany, Bakhsh, Qari, & Maimani, 2012). Byun EJ et al. (Byun, Heo, Cho, Lee, & Kim, 2017) reported a high incidence of deficiency to the recent study as 73.3% in vitamin D3 of the Korean population. Whereas, In the USA, Martineau et al reported a level of 19.9 ng/mL 25(OH) D (Martineau et al., 2017). All previously mentioned results are classified as insufficiency according to the American Geriatric Society (AGS) Classification of Vitamin D3 levels guidelines.

The decreased levels of vitamin D3 in this study could be attributed to conceivable reasons, firstly; the wide age spectrum of the study population as the age range was extending from 2 years up to 80 years. The process of Vit D synthesis is impaired by physiological changes combined with the aging process, for instance, reduced cholecalciferol synthesis in the skin, malabsorption, lower UVB exposure rates, and lower enzymatic activities in liver and kidneys (Laird et al., 2018). The statistical analysis of the study population has revealed a negative correlation between age and serum Vit D levels($r=0.241$, $p<0.01$). The highest Vit D levels were measured in the categories of 2- 10 years which points to a possible effect of the demographical factors as age on reducing levels of Vitamin D3in the other age group. Several studies reported significantly lower levels of vitamin D3 in the elderly than younger ages(Abdul-Razzak, Obeidat, Al-Farras, & Dauod, 2014; Al-Horani et al., 2016; Aleteng et al., 2017). These variations could be attributed to the depressed enzymatic activity corresponding in the synthesis of Vitamin D3 (Jungert & Neuhauser-Berthold, 2013).

Secondly, the study population hada higher percentage of females which conferred a statistical shift to the left in the mean value for the study population as levels of Vitamin D3 were higher in males than females. In line with Nicholas et al study the prevalence of vitamin D3 deficiency was higher for females compared with males (P=0.002) and lower for children 24–35 months of age (P=0.018) compared with children 12–23 months of age (Nichols et al., 2012). Likewise, Millen et al conducted a study 913 women participated, 275 had inadequate levels between 12 and 20 ng/mL, and 88 had deficient levels less than 12 ng/mL (Millen et al., 2015). Aynure et al. (Öztekin & Öztekin, 2018) have reported higher levels of Vitamin D3 in males than females. Al-Horani et al. (Al-Horani et al., 2016), reported a significant difference in the serum levels of vitamin D3 between youth males than females as their mean levels were 25.82 ng/ml and 21.95 ng/mL, respectively.

The reason behind the differences could be attributed to a higher percentage of adipose tissue in females which provides more storage sites for vitamin D3(Abbas, 2017). In our study, there was a significant descending correlation between Vitamin D3 levels and the increase in BMI (.229** P<0.001). Around 59% of females participated in the current study showed obesity and severe obesity. From our study there is a significant correlation between the

BMI and the vitamin D3 serum levels in a negative proportional equivalence (r= -0.229 p<0.001)as the highest levels of Vitamin D3 were measured in 18.5 km2/m categories whereas in the lowest levels were measured in the category of obese > 35 km2/m; regardless to other factors (Table 4). These findings are consistent with Brock et al., summarized the inverse effect of (BMI) over 30 kg/m2 on vitamin D3 levels (Brock et al., 2010). Subjects with normal and overweight BMI have a higher percentage of adipose tissue than less weight subject conferring increment in the bioavailability of vitamin D3(Gislefoss et al., 2018) and this is in concomitant with the results revealed in this study.

Another possible factor for the low Vitamin D3status in females is the lack of skin exposure to sunlight and the Islamic dress (hijab) wearing; a high percentage of the Al-Russeifa society females wear headscarves, long shirts, and trousers which minimizes the exposure area for sunlight. In addition, the females under study reported using sun blocks creams on the facial and hand regions when they perform outdoor activities.

Lastly, Vitamin D3 levels were higher in nonsmokers compared to smokers with an increment proportion of 24.85% regardless ofgender. Interestingly, smoking has significantly impacted the levels of vitamin D3 in a negative manner(r= -0.341 *P*< 0.050). Further analysis for the levels of vitamin D3 in males and females according to smoking habit has revealed higher levels of Vit D in males than females in nonsmoking category (r= 0.33, p= 0.041) whereas there was absolutely no difference in Vit D levels between male and female smokers.

Byun EJ et al. Sebekova K et al. (Sebekova, Krivosikova, Gajdos, & Podracka, 2016) K showed higher levels of vitamin D3 in healthy non-smokers 41±19 ng/ml compared to 30±12 ng/ml for smokers. Jiang et al. (C. Q. Jiang et al., 2016) described the negative correlation of smoking on vitamin D3 levels according to the smoking duration and number of cigarettes consumed per day in China. He reported mean vitamin D3 levels 17.2, 15.0 and 15.4 ng/mL for never, former and current smokers, respectively. Kassi et al demonstrated a significant correlation between both smoking and vitamin D3 (p<0.001) a decrease of about 4.3 ng/dl (p<0.001) in a smoker compared to a non-smoker in levels of vitamin D3 level was lower by approximately among the totality of participants (Kassi et al., 2015).

CONCLUSION

There is a high prevalence of Vitamin D3 deficiency and insufficiency among the Jordanian citizens in Al-Russeifa province. Smoking, age, and BMI are inversely associated with low levels of vitamin D3 in the Jordanian population.

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Conflict of interest

Authors confirm no conflict of interest

REFERENCES

[1] Abbas, M. A. (2017). Physiological functions of Vitamin D in adipose tissue. *J Steroid Biochem Mol Biol, 165*(Pt B), 369-381. doi: 10.1016/j.jsbmb.2016.08.004

[2] Abdul-Razzak, K. K., Obeidat, B. A., Al-Farras, M. I., & Dauod, A. S. (2014). Vitamin D and PTH status among adolescent and young females with severe dysmenorrhea. *J Pediatr Adolesc Gynecol, 27*(2), 78-82. doi: 10.1016/j.jpag.2013.07.005

[3] Abu Rayyan, Walid (2016a). The Impact of Chronic Smoking on Blood and Hair Cadmium Levels among Saudi Citizens in Hail. *Scholars Journal of Applied Medical Sciences, 4*(1C), 244-250.

[4] Abu Rayyan, Walid (2016b). Influence of Smoking Duration on Cadmium Deposition in Blood and Scalp Hair among University Students in Jordan. *Iran J Public Health, 45*(2).

[5] Ahmadieh, H., & Arabi, A. (2011). Vitamins and bone health: beyond calcium and vitamin D. *Nutr Rev, 69*(10), 584-598. doi: 10.1111/j.1753-4887.2011.00372.x

[6] Al-Horani, H., Abu Dayyih, W., Mallah, E., Hamad, M., Mima, M., Awad, R., & Arafat, T. (2016). Nationality, Gender, Age, and Body Mass Index Influences on Vitamin D Concentration among Elderly Patients and Young Iraqi and Jordanian in Jordan. *Biochem Res Int, 2016*, 8920503. doi: 10.1155/2016/8920503

[7] Al Haj Ahmad, R. M., & Al-Domi, H. A. (2017). Vitamin D Insufficiency Predicts Elevated Levels of Complement 3 Independent of Insulin Resistance and BMI. *J Nutr Sci Vitaminol (Tokyo), 63*(3), 155-160. doi: 10.3177/jnsv.63.155

[8] Aleteng, Q., Zhao, L., Lin, H., Xia, M., Ma, H., Gao, J., . . . Gao, X. (2017). Optimal Vitamin D Status in a Middle-Aged and Elderly Population Residing in Shanghai, China. *Med Sci Monit, 23*, 6001-6011.

[9] Alkhatatbeh, M. J., Abdul-Razzak, K. K., Khasawneh, L. Q., & Saadeh, N. A. (2017). High Prevalence of Vitamin D Deficiency and Correlation of Serum Vitamin D with Cardiovascular Risk in Patients with Metabolic Syndrome. *Metab Syndr Relat Disord, 15*(5), 213-219. doi: 10.1089/met.2017.0003

[10] American Geriatrics Society Workgroup on Vitamin D Supplementation for Older Adults, AGS. (2014). Recommendations abstracted from the American geriatrics society consensus statement on vitamin D for prevention of falls and their consequences. *Journal of the American Geriatrics Society, 62*(1), 147-152.

[11] Ardawi, M. S., Sibiany, A. M., Bakhsh, T. M., Qari, M. H., & Maimani, A. A. (2012). High prevalence of vitamin D deficiency among healthy Saudi Arabian men: relationship to bone mineral density, parathyroid hormone, bone turnover markers, and lifestyle factors. *Osteoporos Int, 23*(2), 675-686. doi: 10.1007/s00198-011-1606-1

[12] Atoum, M. F., AlKateeb, D., & AlHaj Mahmoud, S. A. (2015). The Fok1 vitamin D receptor gene polymorphism and 25(OH) D serum levels and prostate cancer among Jordanian men. *Asian Pac J Cancer Prev, 16*(6), 2227-2230.

[13] Bouillon, Roger. (2017). Genetic and racial differences in the vitamin D endocrine system. *Endocrinology and Metabolism Clinics, 46*(4), 1119-1135.

[14] Brock, K. E., Graubard, B. I., Fraser, D. R., Weinstein, S. J., Stolzenberg-Solomon, R. Z., Lim, U., . . . Albanes, D. (2010). Predictors of vitamin D biochemical status in a large sample of middle-aged male smokers in Finland. *Eur J Clin Nutr, 64*(3), 280-288. doi: 10.1038/ejcn.2009.137

[15] Brum, D. G., Comini-Frota, E. R., Vasconcelos, C. C., & Dias-Tosta, E. (2014). Supplementation and therapeutic use of vitamin D in

patients with multiple sclerosis: consensus of the Scientific Department of Neuroimmunology of the Brazilian Academy of Neurology. *Arq Neuropsiquiatr, 72*(2), 152-156. doi: 10.1590/0004-282X20130252

[16] Byun, E. J., Heo, J., Cho, S. H., Lee, J. D., & Kim, H. S. (2017). Suboptimal vitamin D status in Korean adolescents: a nationwide study on its prevalence, risk factors including cotinine-verified smoking status and association with atopic dermatitis and asthma. *BMJ Open, 7*(7), e016409. doi: 10.1136/bmjopen-2017-016409

[17] Carmeliet, Geert, Dermauw, Veronique, & Bouillon, Roger. (2015). Vitamin D signaling in calcium and bone homeostasis: a delicate balance. *Best Practice & Research Clinical Endocrinology & Metabolism, 29*(4), 621-631.

[18] Chinellato, I., Piazza, M., Sandri, M., Paiola, G., Tezza, G., & Boner, A. L. (2018). Correlation between vitamin D serum levels and passive smoking exposure in children with asthma. *Allergy Asthma Proc, 39*(3), 8-14. doi: 10.2500/aap.2018.39.4124

[19] Dawson-Hughes, Bess. (2014). Vitamin D deficiency in adults: Definition, clinical manifestations, and treatment. *UpToDate, Waltham, MA. Accessed, 3*.

[20] Dzik, Katarzyna Patrycja, & Kaczor, Jan Jacek. (2019). Mechanisms of vitamin D on skeletal muscle function: oxidative stress, energy metabolism and anabolic state. *European journal of applied physiology, 119*(4), 825-839.

[21] Freedman, B. I., Divers, J., Russell, G. B., Palmer, N. D., Wagenknecht, L. E., Smith, S. C., Register, T. C. (2015). Vitamin D Associations With Renal, Bone, and Cardiovascular Phenotypes: African American-Diabetes Heart Study. *J Clin Endocrinol Metab, 100*(10), 3693-3701. doi: 10.1210/jc.2015-2167

[22] Gislefoss, R. E., Stenehjem, J. S., Hektoen, H. H., Andreassen, B. K., Langseth, H., Axcrona, K., . . . Robsahm, T. E. (2018). Vitamin D, obesity and leptin in relation to bladder cancer incidence and survival: prospective protocol study.

BMJ Open, 8(3), e019309. doi: 10.1136/bmjopen-2017-019309

[23] Heulens, N., Korf, H., Cielen, N., De Smidt, E., Maes, K., Gysemans, C., . . . Janssens, W. (2015). Vitamin D deficiency exacerbates COPD-like characteristics in the lungs of cigarette smoke-exposed mice. *Respir Res, 16*, 110. doi: 10.1186/s12931-015-0271-x

[24] Jarrah, M. I., Mhaidat, N. M., Alzoubi, K. H., Alrabadi, N., Alsatari, E., Khader, Y., & Bataineh, M. F. (2018). The association between the serum level of vitamin D and ischemic heart disease: a study from Jordan. *Vasc Health Risk Manag, 14*, 119-127. doi: 10.2147/VHRM.S167024

[25] Jia, J., Shen, C., Mao, L., Yang, K., Men, C., & Zhan, Y. (2014). Vitamin D receptor genetic polymorphism is significantly associated with decreased risk of hypertension in a Chinese Han population. *J Clin Hypertens (Greenwich), 16*(9), 634-639. doi: 10.1111/jch.12386

[26] Jiang, C. Q., Chan, Y. H., Xu, L., Jin, Y. L., Zhu, T., Zhang, W. S., . . . Lam, T. H. (2016). Smoking and serum vitamin D in older Chinese people: cross-sectional analysis based on the Guangzhou Biobank Cohort Study. *BMJ Open, 6*(6), e010946. doi: 10.1136/bmjopen-2015-010946

[27] Jiang, Xia, O'Reilly, Paul F, Aschard, Hugues, Hsu, Yi-Hsiang, Richards, J Brent, Dupuis, Josée, . . . Berry, Diane. (2018). Genome-wide association study in 79,366 European-ancestry individuals informs the genetic architecture of 25-hydroxyvitamin D levels. *Nature communications, 9*(1), 260.

[28] Jungert, A., & Neuhauser-Berthold, M. (2013). Dietary vitamin D intake is not associated with 25-hydroxyvitamin D3 or parathyroid hormone in elderly subjects, whereas the calcium-to-phosphate ratio affects parathyroid hormone. *Nutr Res, 33*(8), 661-667. doi: 10.1016/j.nutres.2013.05.011

[29] Jungert, A., Roth, H. J., & Neuhauser-Berthold, M. (2015). Associations of serum 25-hydroxycholecalciferol and parathyroid hormone with serum lipids differ by sex and vitamin D status. *Public Health Nutr, 18*(9),

1684-1691. doi: 10.1017/S1368980014002286

[30] Kassi, E. N., Stavropoulos, S., Kokkoris, P., Galanos, A., Moutsatsou, P., Dimas, C., . . . Lyritis, G. (2015). Smoking is a significant determinant of low serum vitamin D in young and middle-aged healthy males. *Hormones (Athens), 14*(2), 245-250. doi: 10.14310/horm.2002.1521

[31] Laird, E., O'Halloran, A. M., Carey, D., Healy, M., O'Connor, D., Moore, P., . . . Kenny, R. A. (2018). The Prevalence of Vitamin D Deficiency and the Determinants of 25(OH)D Concentration in Older Irish Adults: Data From The Irish Longitudinal Study on Ageing (TILDA). *J Gerontol A Biol Sci Med Sci, 73*(4), 519-525. doi: 10.1093/gerona/glx168

[32] Lavie, Carl J, Carbone, Salvatore, Kachur, Sergey, O'keefe, Evan L, & Elagizi, Andrew. (2019). Effects of Physical Activity, Exercise, and Fitness on Obesity-Related Morbidity and Mortality. *Current sports medicine reports, 18*(8), 292-298.

[33] Li, Yatong, Hui, Min, Chang, Xiao, Li, Mei, Wang, Yipeng, Zhang, Baozhong, & Yu, Jianchun. (2018). BMI reduction and vitamin D insufficiency mediated osteoporosis and fragility fractures in patients at nutritional risk: a cross-sectional study. *European journal of clinical nutrition, 72*(3), 455.

[34] Macdonald, HM, Mavroeidi, A, Fraser, WD, Darling, AL, Black, AJ, Aucott, L, . . . Lanham-New, SA. (2011). Sunlight and dietary contributions to the seasonal vitamin D status of cohorts of healthy postmenopausal women living at northerly latitudes: a major cause for concern? *Osteoporosis International, 22*(9), 2461-2472.

[35] Mallah, Eyad, Rayyan, Walid Abu, Dayyih, Wael Abu, Al-Majali, Ibrahim S, Qaralleh, Haitham, & Al-Thunibat, Osama Yosef. (2018). Analytical and Comparative Study About the Impact of Lead Homeostasis on Cardiovascular Disorders in Humans. *Biomedical and Pharmacology Journal, 11*(1), 277-284.

[36] Martineau, Adrian R, Jolliffe, David A, Hooper, Richard L, Greenberg,

Lauren, Aloia, John F, Bergman, Peter, . . . Ginde, Adit A. (2017). Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *bmj, 356*, i6583.

[37] Millen, A. E., Meyers, K. J., Liu, Z., Engelman, C. D., Wallace, R. B., LeBlanc, E. S., . . . Mares, J. A. (2015). Association between vitamin D status and age-related macular degeneration by genetic risk. *JAMA Ophthalmol, 133*(10), 1171-1179. doi: 10.1001/jamaophthalmol.2015.2715

[38] Nichols, E. K., Khatib, I. M., Aburto, N. J., Serdula, M. K., Scanlon, K. S., Wirth, J. P., & Sullivan, K. M. (2015). Vitamin D status and associated factors of deficiency among Jordanian children of preschool age. *Eur J Clin Nutr, 69*(1), 90-95. doi: 10.1038/ejcn.2014.142

[39] Nichols, E. K., Khatib, I. M., Aburto, N. J., Sullivan, K. M., Scanlon, K. S., Wirth, J. P., & Serdula, M. K. (2012). Vitamin D status and determinants of deficiency among non-pregnant Jordanian women of reproductive age. *Eur J Clin Nutr, 66*(6), 751-756. doi: 10.1038/ejcn.2012.25

[40] Öztekin, Aynure, & Öztekin, Coşkun. (2018). Vitamin D levels in patients with recurrent aphthous stomatitis. *BMC Oral Health, 18*(1), 186.

[41] Sebekova, K., Krivosikova, Z., Gajdos, M., & Podracka, L. (2016). Vitamin D status in apparently healthy medication-free Slovaks: Association to blood pressure, body mass index, self-reported smoking status and physical activity. *Bratisl Lek Listy, 117*(12), 702-709. doi: 10.4149/BLL_2016_135

[42] Talhout, Reinskje, Schulz, Thomas, Florek, Ewa, Van Benthem, Jan, Wester, Piet, & Opperhuizen, Antoon. (2011). Hazardous compounds in tobacco smoke. *International journal of environmental research and public health, 8*(2), 613-628.

[43] Underner, M, Peiffer, G, Perriot, J, Harika-Germaneau, G, & Jaafari, N. (2018). Is reduction of tobacco consumption associated with reduced risk of cardiovascular and pulmonary mortality and morbidity?

Revue de pneumologie clinique, 74(3), 188-195.

[44] van Duijnhoven, F. J. B., Jenab, M., Hveem, K., Siersema, P. D., Fedirko, V., Duell, E. J., . . . Bueno-de-Mesquita, H. B. A. (2018). Circulating concentrations of vitamin D in relation to pancreatic cancer risk in European populations. *Int J Cancer, 142*(6), 1189-1201. doi: 10.1002/ijc.31146

[45] Wang, Yongji, Zhu, Jinge, & DeLuca, Hector F. (2012). Where is the vitamin D receptor? *Archives of biochemistry and biophysics, 523*(1), 123-133.

[46] Yoshihara, A., Kaneko, N., Iwasaki, M., Nohno, K., & Miyazaki, H. (2018). Relationship between vitamin D receptor gene polymorphism and susceptibility to chronic kidney disease and periodontal disease in community-dwelling elderly. *J Clin Periodontol, 45*(6), 672-679. doi: 10.1111/jcpe.12896